#33
11-14-02

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Appellants: Merton Bernfield and Ofer Reizes

Serial No:	08/965,356	Art Unit:	1632
Filed:	November 6, 1997	Examiner:	A. Baker

For: METHODS AND REAGENTS FOR REGULATING OBESITY

Assistant Commissioner for Patents
Washington, D.C. 20231

REPLY TO EXAMINER'S ANSWER

Sir:

This is a Reply to the Examiner's Answer mailed February 27, 2001. Enclosed is a Request for Oral Hearing, and the appropriate fee for a small entity, as well as an Amendment to the Claims.

(3) STATUS OF CLAIMS ON APPEAL

The examiner is correct that claims 1, 3, 4, 5, 6, 10, 12, 13, 14 and 15 are pending. The accompanying amendment amends claims 6 and 15 into independent form and removes them from appeal. Claims 1, 3-5, 10, and 12-14 are on appeal. The text of each claim on appeal, as amended, is set forth in the Appendix to this Appeal Brief.

(6) ISSUES ON APPEAL

The issue presented on appeal is whether claims 1, 3-5, 10, and 12-14 should be rejected under 35 U.S.C. § 112, first paragraph, as not enabling for transgenic rodents having the defined phenotype.

(7) GROUPING OF CLAIMS

The examiner has argued that appellants did not provide reasons for the claims standing or falling separately. This is not true. Appellants believe the claims drawn to the transgenic rodents should be examined separately from the claims to methods for using the transgenic rodents, based on the belief that animals other than those defined by claims 1 and 3-6 could be used in the screening methods of claims 10 and 13-15.

Claims 1 and 3-6 are drawn to transgenic rodents. Claim 5 requires that the transgene incorporates the cytomegalovirus promoter and the cytomegalovirus intermediate/early enhancer. Claim 6 specifies a particular genotype, FVB/N-TgN(synd-1).

Claims 10 and 13-15 are drawn to methods for screening of compounds which can alter body weight, by administering the compounds to be screened to an animal as defined by claims 1 and 3-6.

The rejection on appeal is based on the premise that examples showing that different lines of transgenic mice can be made which exhibit the claimed phenotype does not support enablement of claims which encompass transgenic rats made with the same constructs which exhibit the claimed phenotype.

(8) ARGUMENTS

The examiner's first point is that the application provides "no guidance is provided in the specification for the preparation and use of any transgenic rodent other than mice." This is simply not accurate. Page 12, line 7 to page 13, line 24, clearly describes microinjection techniques which are generally applicable to a variety of species. "Although the study described herein used mice, it would clearly be routine to apply the same technology to other rodents such as rats or hamsters, or even to larger animals such as sheep, pigs, or goats" (page 12, lines 11-13). These statements are fully supported by the enclosed abstract of Charreau, et al., "Transgenesis in rats: technical aspects and models" Transgenic Res. 5(4):223-2334 (1996). There is no indication that the "use" would be any different for a transgenic rat or rabbit than for a mouse.

Accordingly, those skilled in the art would have had no trouble making and using the claimed animals.

The examiner's second basis for rejecting the claims was that one skilled in the art would have no expectation that one could obtain the claimed animals using the disclosed methods and reagents. The appellants, who are highly skilled in the study of obesity, proteoglycans, and making and using transgenic animals, provided their opinion that studies done to make and screen compounds using genetically engineered mice are predictable of the same results in rats. Several articles were submitted to demonstrate that results obtained with mice are predictive of results obtained with rats. Papers were also provided that showed that those skilled in the field of obesity and of transgenic rodents, routinely make the same genetic changes to both rats and mice, and observe the same phenotypes in response. See for example, studies reported for diabetic mice and rats, mice and rats with high fat induced hyperleptinemia, VMH lesioned mice

and rats, and genetic defects resulting in obesity (Frederich, et al., Natl. Med. 1(12):1311-1314 (1995) (mice); Surwit, et al., Diabetes 46(9):1516-1520 (1997) (mice); Suga, et al., Am. J. Physiol. Endocrinol. Metab. 278(4):E677-683 (2000) (rats); Wang, et al., Biochem. Biophys. Res. Commun. 277(1):20-26 (2000) (rats); Wang, et al., Proc. Natl. Acad. Sci. USA 96(18):10373-10378 (1999) (rats)).

The examiner's response to this evidence has been to point again to the literature cited as allegedly creating a prima facie case of non-enablement. It is not essential to decide whether or not the examiner has succeeded in making a prima facie case since the appellants have provided substantially more evidence in rebuttal that the examiner is simply not correct when one is speaking, at least in this case, of animal models for obesity. The examiner provided nothing in rebuttal to the evidence that the appellants have provided, nor any reply to appellants' reasoned statements as to why her characterization of the art does not apply in this case.

The standard for making a rejection based on 35 U.S.C. § 112, first paragraph is articulated in *In re Wands*, 858 F.2d 731 (Fed. Cir. 1988) (see also MPEP § 2164.01 and 2164.04). Initially, the Patent Office must accept the objective truth of statements made in the specification. If such statements are to be called into question, the Patent Office is burdened with providing evidence or convincing argument why those of skill in the art would doubt the statements (*In re Marzocchi*, 439 F.2d 220, 169 USPQ 367 (CCPA 1971)). Applicants are only required to describe the claimed invention in sufficient detail to enable those of skill in the art to make and use it without the need for undue experimentation. Appellants submit that this has been done.

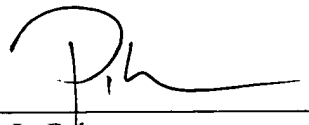
It is well established that the examiner can rebut the presumption that an application as filed is enabling. It is just as well established that the applicant can provide evidence in reply. In

this case, the appellants have provided evidence in reply to the examiner's literature support of her position, and nothing has been provided to rebut their evidence. In this case the presumption of enablement must stand.

In summary, appellants have provided an abundance of evidence showing that the claims are enabled for rodents expressing a stably integrated syndecan which exhibit maturity onset obesity: demonstrating that animals expressing syndecan from DNA inserts at different points and in different numbers still exhibit the same phenotype; that normal animals can have their syndecan levels manipulated merely by diet (again showing that it is the expressed syndecan, not the point of insertion of the transgene that is critical), that mice and rats are made using the same materials and techniques, without undue experimentation, and that at least in the field of obesity, mice and rats are interchangeable models and predictive of results to be obtained in each species. The examiner has failed to provide any evidence to rebut this proof. Therefore the claims are enabled under 35 U.S.C. §112.

Allowance of all claims 1, 3-6, 10, 12 and 13-15 as fully enabled by the specification is earnestly solicited.

Respectfully submitted,



Patrea L. Pabst
Reg. No. 31,284

Date: April 27, 2001
ARNALL GOLDEN & GREGORY, LLP
2800 One Atlantic Center
1201 West Peachtree Street
Atlanta, Georgia 30309-3450
(404) 873-8794
(404) 873-8795 Telefax

CERTIFICATE OF MAILING (37 CFR 1.8)

I hereby certify that this Appeal Brief, along with any paper referred to as being attached or enclosed, is being deposited with the U.S. Postal Service on the date shown below with sufficient postage as first-class in an envelope addressed to the Assistant Commissioner for Patents, Washington, D.C. 20231.

Date: April 27, 2001

Patrea L. Pabst

APPENDIX: Claims as pending on appeal upon entry of accompanying Amendment

1. A transgenic rodent whose genome comprises a stably integrated DNA sequence encoding a syndecanoperably linked to a promoter, wherein expression of the DNA sequence results in the rodent developing maturity onset obesity.

3. The rodent of claim 1 wherein the DNA sequence encodes syndecan -1.

4. The rodent of claim 1 wherein the syndecan is expressed in the areas of the hypothalamus responsible for the regulation of body weight and energy balance.

5. The rodent of claim1 where the promoter is a cytomegalovirus promoter or functional portion thereof, and the CMV intermediate/early enhancer.

6. A transgenic rodent whose genome comprises a stably integrated DNA sequence encoding a syndecan operably linked to a promoter, wherein expression of the DNA sequence results in the rodent developing maturity onset obesity having the genotype FVB/N-TgN(synd-1).

10. A method for screening for compounds which can alter body weight comprising:

administering a compound to a transgenic rodent whose genome comprises a stably integrated DNA sequence encoding a syndecan operably linked to a promoter, wherein expression of the DNA sequences results in the rodent developing maturity onset obesity, and

observing whether there is a change in body weight over a period of time.

12. The method of claim 10 wherein the syndecan is syndecan-1.

13. The method of claim 10 wherein the syndecan is expressed in the areas of the hypothalamus responsible for the regulation of body weight and energy balance.

14. The method of claim 10 wherein the promoter is a cytomegalovirus promoter or functional portion thereof, and the CMV intermediate/early enhancer.

15. A method for screening for compounds which can alter body weight comprising:

administering a compound to a transgenic rodent whose genome comprises a stably integrated DNA sequence encoding a syndecan operably linked to a promoter, wherein expression of the DNA sequences results in the rodent developing maturity onset obesity, and

observing whether there is a change in body weight over a period of time,

wherein the rodent has the genotype FVB/N-TgN(synd-1).

Entrez PubMed
Overview
Help | FAQ
Tutorial NEW
New/Noteworthy

PubMed Services
Journal Browser
MeSH Browser
Single Citation Matcher
Batch Citation Matcher
Clinical Queries
Cubby

Related Resources
Order Documents
Grateful Med
Consumer Health
Clinical Alerts
ClinicalTrials.gov

Privacy Policy

1: Transgenic Res 1996 Jul;5(4):223-34 Related Articles, Boo

Transgenesis in rats: technical aspects and models.

Charreau B, Tesson L, Soulillou JP, Pourcel C, Anegon I.

INSERM U437, Institut de Transplantation et Recherche en Transplantation, Nantes, France.

The production of transgenic rats by DNA-microinjection into fertilized ova has now become an established procedure, although fewer than 20 lines hav been described during the last 5 years. Overall, transgenic rats remain more difficult to produce than transgenic mice, but satisfactory yields have been obtained by several laboratories. A review of the methods used to generate transgenic rats shows considerable variation between different laboratories, particularly in choice of strain, superovulation protocols and the use of embryo culture before reimplantation. In some instances, the production of transgenic rats has provided data that are new and relevant, compared to dat obtained in mice bearing the same transgene. Models have been developed f human diseases such as hypertension and autoimmunity, and applications have been found in the study of carcinogenesis and in pharmacological research. Transgenic rat technology also opens up interesting perspectives fo transplantation research, in which microsurgery is an essential procedure. Intensive research is in progress in several laboratories to produce rat embryonic stem (ES) cell lines, but existing lines have not participated in germ line formation a prerequisite for their use in gene knock out experiments.

Publication Types:
- Review
- Review, tutorial

PMID: 8755162 [PubMed - indexed for MEDLINE]